Women and Ischemia Syndrome Evaluation (WISE)
Diagnosis and Pathophysiology of Ischemic Heart Disease
Workshop

October 2-4, 2002

Session 5

1. Topic and Author

Gender Related Risk Factors for IHD: Novel Risk Factors
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2. Where we stand in 2002. Overview/rationale for inclusion of topic.

A number of new (novel?) risk factors for IHD have been introduced over the past 10 years[1]. These have ranged from new forms of lipid particles, to metabolites, to hemostatic factors, to inflammation markers. Some of these have stood the test of multiple positive studies, while others have not. In many cases they are related and in some cases tightly related. Also, they are commonly related to the set of abnormalities we call the Metabolic Syndrome. This inter-relatedness causes two problems: a) it is often uncleart which marker might best represent the group; and b) it is difficult to identify the independent effects of each marker.

Blood proteins associated with inflammation have proven to be consistent risk factors for heart disease in both men and women[2]. The most-studied markers in this class are C-ractive protein, fibrinogen and IL6. These markers are largely independent of lipid effects[3], but are closely related to insulin resistance[4] and adiposity[5]; fibrinogen in particular reflects age[6] and other measures of existing heart diease[7]. They are also related to coagulation activity, IL-6 and CRP[8] more than fibrinogen. To a certain extent they reflect underlying atherosclerotic disease (fibrinogen[7] more than CRP[8]), but this relatively weak association[9] wouldn't appear to account for all, or even most, of their predictive power. While these markers may add independent effects in prediction models which have been fully adjusted for other CVD risk factors, the incremental predictive power is small. However, they can summarize much of the predictive in some other "traditional" risk factors, so that two component risk models (e.g., lipids and CRP[3]) are quite powerful in prediction.

These associations with heart disease appear to be true for across the life span for both men and women, although predominantly for men in older age groups[10]. Some medications have relatively large effects, which may affect the relationship of the marker to disease. For example, post-menopausal estrogen can increase CRP levels 2-3 fold[11]. The relationship of this effect to actual risk remains unclear. Interestingly, fibrinogen is unaffected by estrogen, or even lowered a bit[12], highlighting that these markers are not all equivalent in all dimensions. It is likely that these markers both reflect underlying pathoplogical processes, and contribute to them as well[13].

3. Current challenges and the most important issues for future research

What is the best marker, and can it (they) be effectively used in risk prediction?
What are these markers telling us about the underlying pathophysiology and new targets for intervention or prevention?
CVD appears different in some ways in older men and older women; what is the underlying issue(s)?

4. Current challenges in the areas of communicating messages to health care community, patients and the public

The systems we dezcribe as "novel" risk markers are in fact our own defense mechanisms against the "world". For example, blood clotting – it may cause a fatal MI, but we can't live without it. This a complex web or relationships posing real educational challeneges.

5. Translating new findings to improved diagnosis and treatment/saving lives.

the obvious target is risk prediction; also, medication use may be helped by measuring these markers.

6. References.

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